CASWELL FILE

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

APR 10 1989

MEMORANDUM

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: 2,4-D: Requests for Waiver from Mutagenicity Testing for 2,4-D and Derivatives

TO: Larry Schnaubelt PM-23
Registration Division (H7505C)

FROM: K. Clark Swentzel K. Clark Swentzel 4/5/89
Acting Section Head
Toxicology Branch II (HFAS)
HED (H7509C)

THRU: Marcia van Gemert, Ph.D. Marcia van Gemert 4/10/89
Acting Branch Chief
Toxicology Branch II (HFAS)
HED (H7509C)

EPA ID Nos.: 50534-13, -14, -102: 464-453, -458, -467
Project No.: 9-1143
Caswell No.: 315

Action Requested

Evaluate and respond to request for waivers from mutagenicity testing. Specifically, 1) a request from the 2,4-D Task Force for a waiver from the requirement to perform testing in the category Other Mechanisms of Mutagenicity on the acid, DMA and IOE forms of 2,4-D and 2) a request from Formenta for a waiver to perform testing in the gene mutation and structural chromosomal aberration categories for their products containing 2,4-D and N-oleyl-1,3-propylenediamine salt of 2,4-D.

Response

TB does not concur with the request from the 2,4-D Task Force (see attached EPA Memorandum, Dearfield, HED, to Rice, RD), however, the request from Formenta involves a chemistry issue that must be resolved before a conclusive response from TB can be provided. Formenta contends that the N-oleyldiamine salt of 2,4-D, which is formed during the formulation process for Dacamine 4D, "has never been isolated nor is it ever isolated in the process of formulation of the Dacamine products," therefore, it is neither a technical active ingredient nor a manufacturing product. On this basis, Formenta proposed that mutagenicity studies should be done on the formulated product, rather than the noted diamine salt of 2,4-D. TB does not object to this proposal provided that DEB concurs with Formenta's statements regarding the isolation of the N-oleyldiamine salt of 2,4-D. However, all three categories of mutagenicity testing must be fulfilled as indicated in the attached memorandum (Dearfield to Rice).

cc. Dick Schmidt - DEB -

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of requests for waiver from mutagenicity testing for 2,4-D and derivatives (HED Project #9-1143)

FROM: Kerry L. Dearfield, Ph.D. Kerry L Dearfield 3.29.89
Geneticist
Science Support Section
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: Chris Rice
Registration Division (H7505C)

THRU: John A. Quest, Ph.D. E. Rinde 3/29/89 3/30/89
Chief
Science Support Section
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

2,4-D [94-75-7] Caswell #315

This reviewer was requested by Registration Division to examine the request for waiver from mutagenicity testing for several 2,4-D derivatives. Two requests were actually in the package sent to HED: 1) a request from the 2,4-D Task Force for a waiver from the requirement to perform testing in the category Other Mechanisms of Mutagenicity on the acid, DMA and IOE forms of 2,4-D; 2) a request from Formenta for a waiver to perform testing in the gene mutation and structural chromosomal aberration categories for their products containing 2,4-D and N-oleyl-1,3-propylenediamine salt of 2,4-D. This response will address both of these requests in order.

1) 2,4-D Task Force request

It is not agreed with the rationale presented by the Task Force that testing in the gene mutation and structural chromosomal aberration categories of mutagenicity testing is sufficient to satisfy the requirements for mutagenicity testing. Part 158 of 40CFR specifically requires mutagenicity testing in all three categories of testing: gene mutation, structural chromosomal aberrations and other genotoxic effects. Since there were no scientific rationale or data to argue against testing in all three categories, this request should be denied. This lack of scientific information becomes even more apparent as it is shown in the

reregistration standard for 2,4-D that there were no acceptable mutagenicity studies submitted to OPP for review. Furthermore, with a cursory examination of the literature on 2,4-D, there are positive effects associated with 2,4-D in the other genotoxic effects category (e.g. the Supplement 6 of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans reports that 2,4-D induced positive responses in an unscheduled DNA synthesis test with cultured human cells and sister chromatid exchanges and aberrations in cultured human lymphocytes). Based on this limited information, there appears to be a mutagenicity concern for 2,4-D that needs to be fully investigated.

2) Formenta request

Formenta suggests that mutagenicity testing in the gene mutation and structural chromosomal aberrations categories (they did not mention the third category of testing for other genotoxic effects, which is a requirement also) would not be applicable since their 2,4-D amine salt does not exist as a technical or manufacturing product and they would have to test the end-use formulation, Dacamine 4D. The issue of what to test is not the specific issue for this reviewer to resolve. If it is decided to test the formulation and/or to isolate and test the N-oleyldiamine salt of 2,4-D, then all three categories of mutagenicity testing must be fulfilled, particularly, as indicated above, 2,4-D itself may present a mutagenicity concern and since there is no mutagenicity data on the amine moiety available to OPP.

cc: Clark Swentzel

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R116972

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